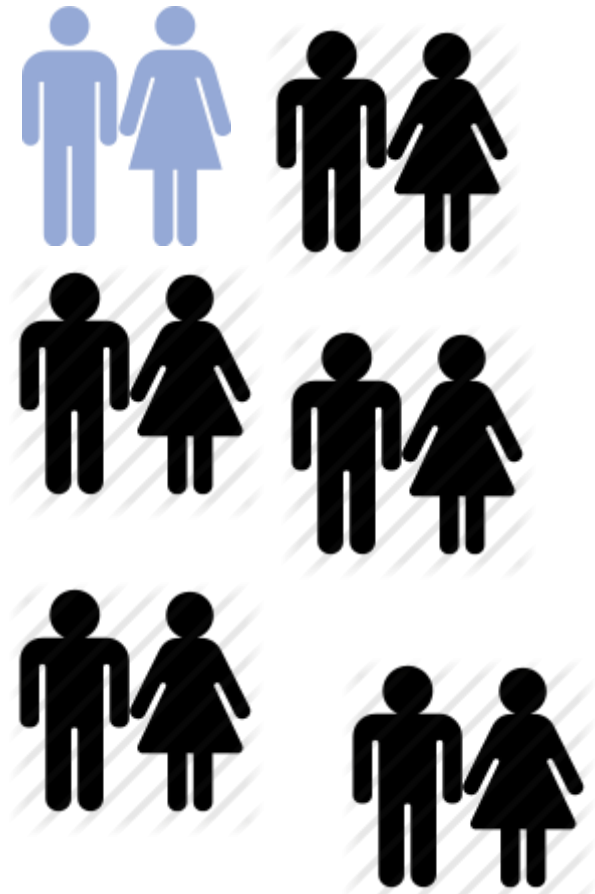


Drugs used in infertility

Lecture-6-
Reproductive Block
Ahlam Sultan

Infertility

- Infertility is define as the inability to conceive a child after 12 months of attempting pregnancy
- Women older than 35 years old may be considered infertile after 6 months
- It remains a major clinical and social problem, affecting perhaps one couple in six
- The most common causes of infertility are:
 1. **Male factor** such as sperm abnormalities
 2. **Female factor** such as ovulation dysfunction and tubal pathology
 3. **Combined** male and female factors
 4. **unexplained** infertility



Causes of Infertility

Female causes

58%

Amenorrhea/
ovulatory
dysfunction

46%

Tubal defect
38%

Endometriosis
9%

Other
7%

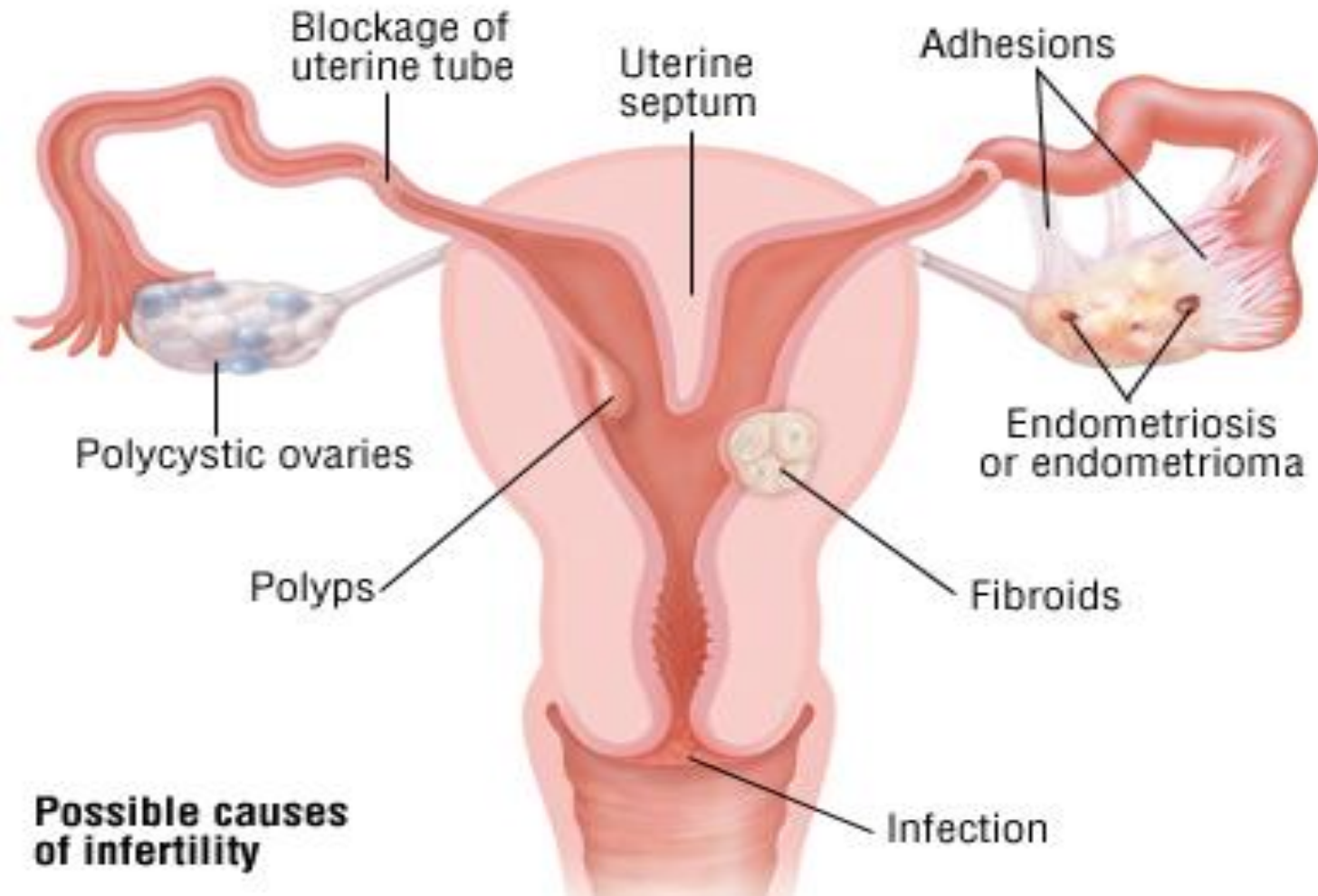
Hypothalamic/
pituitary
causes
51%

Polycystic
ovary
syndrome
30%

Premature
ovarian
failure
12%



Causes of Infertility



Causes of Infertility

Male causes

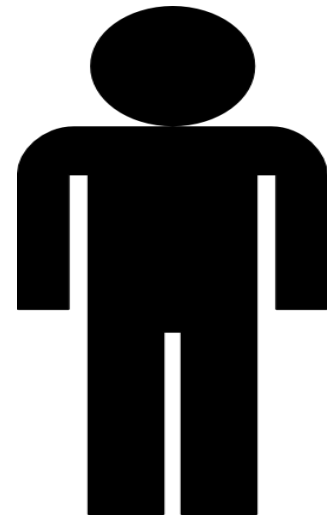
25%

Primary
hypogonadism
(↑FSH)
30-40%

Secondary
hypogonadism
(↓ FSH, ↓ LH)
2%

Disordered sperm
transport
10-20%

Unknown
40-50%



Treatment of infertility

- Non-pharmacological measures:

- ✓ Stop smoking
- ✓ Reduce weight (obesity is associated with infertility in both men and women)
- ✓ Women should stop intensive exercise
- Treatment of infertility should be **tailored** to the problems unique to each couple

- A **stepwise treatment approach** to infertility is optimal, beginning with low-risk interventions and moving to more invasive, higher risk interventions only if necessary
- The time used to complete the evaluation, correction, and expectant management can be longer in women aged < 30 years, but **this process should be advanced rapidly in women age > 35 years**

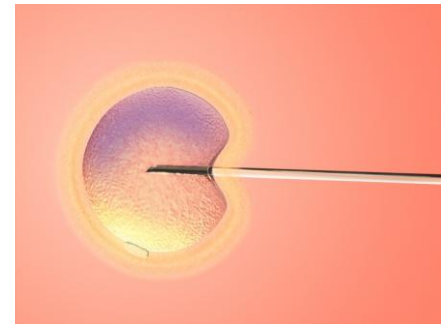
Treatment of Ovulations disorder

Ovulatory disorders

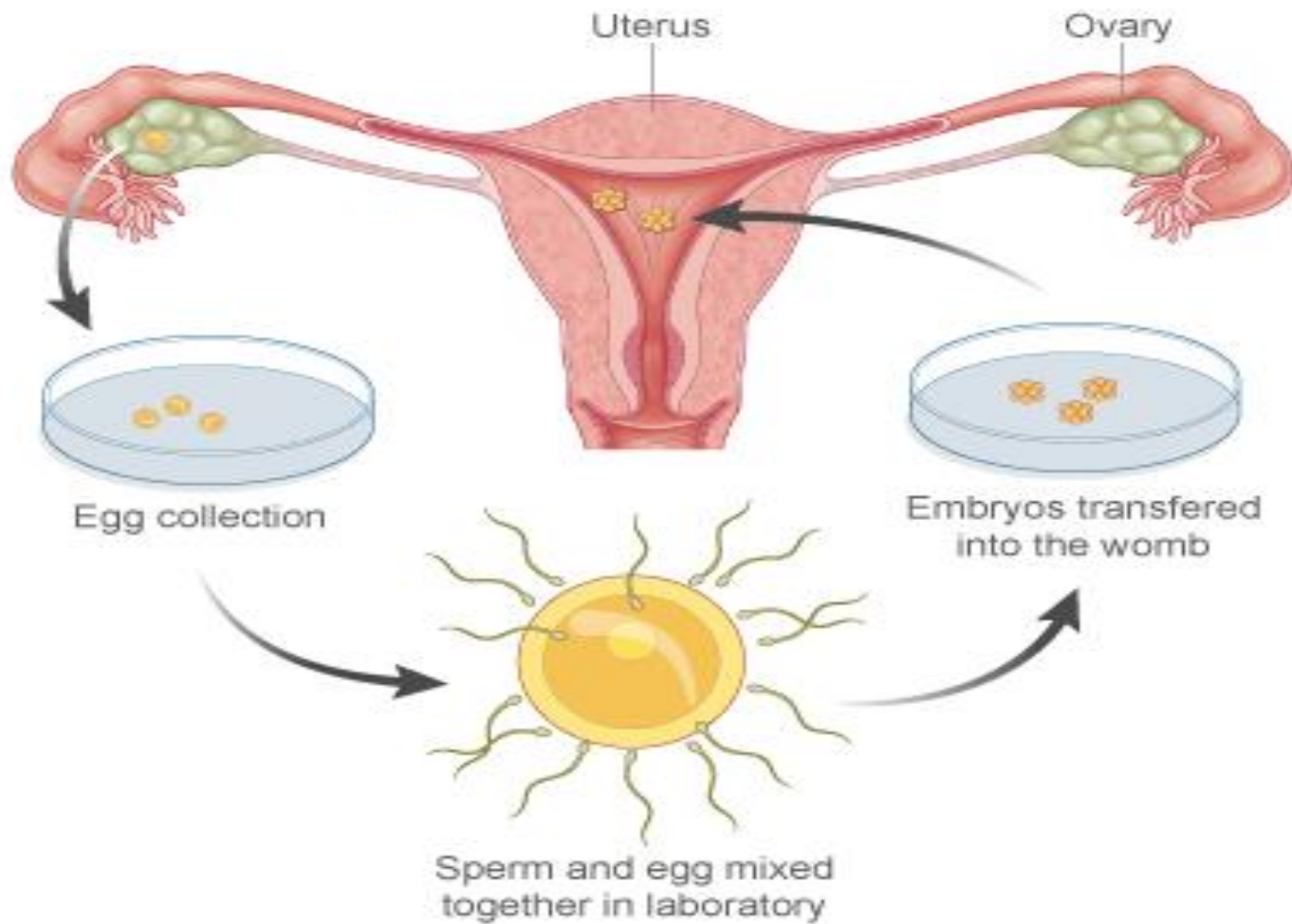
- Amenorrhoea
- Oligo-ovulation
- Hyperprolactinaemia
- Polycystic ovaries syndrome (PCOS)

Treatment:

- Clomiphene citrate
- Gonadotrophins
- Metformin + clomiphene
- Bromocriptine (**for hyperprolactinaemia ONLY**)
- Laparoscopic ovarian diathermy
- In-vitro fertilization (IVF)



IVF



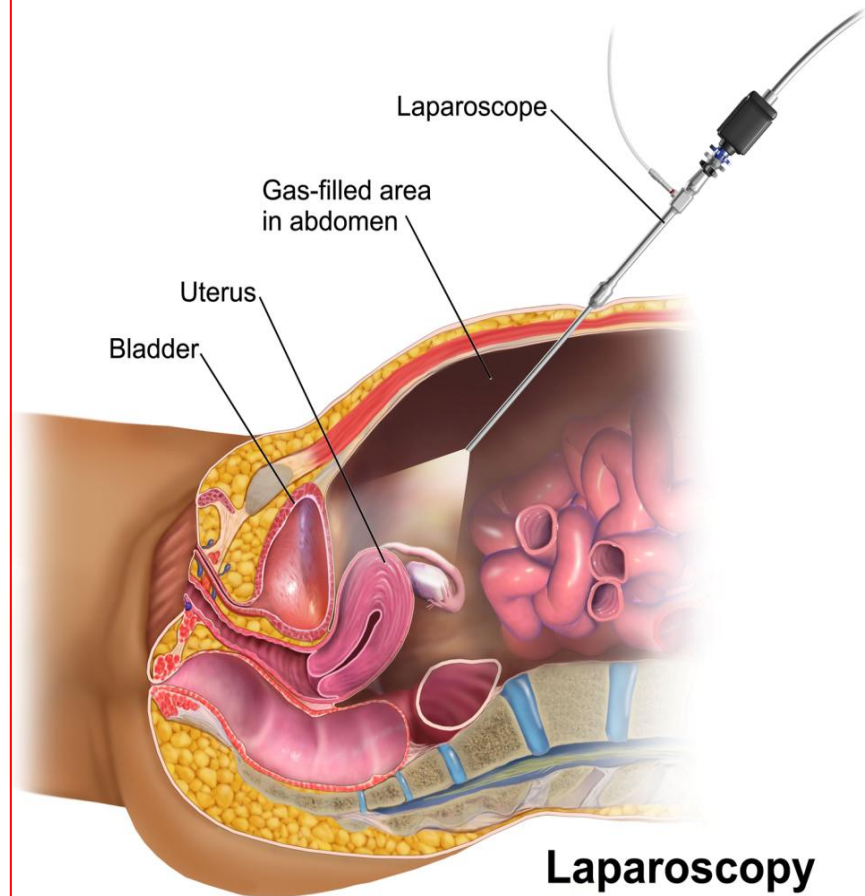
Treatment of Tubal disease

Pelvic disorders:

- Tubal obstruction
- Other tubal defect

☐ **Fallopian tube obstruction** is a major cause of female infertility. Blocked fallopian tubes are unable to let the ovum and the sperm converge, thus making fertilization impossible.

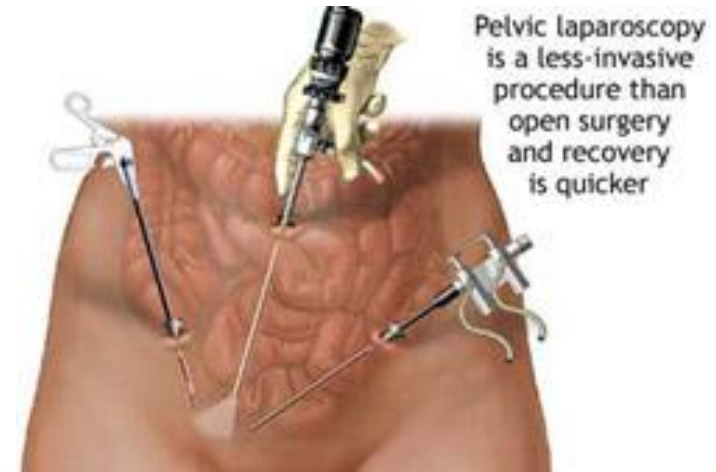
✓ These patients are at higher risk of developing an ectopic pregnancy.



Tubal disease

Treatment by:

- **Tubal surgery** (Tubal reconstruction may be attempted if tubal disease is identified)
- **Laparoscopy with tubal lavage** is recommended in case of: hysterosalpingography suggests a tubal or uterine cavity abnormality
- **IVF**



Laparoscopy



Treatment of Endometriosis

- Endometriosis stages I, II, III and IV
- 60% with minimal or mild endometriosis may conceive within 1 year without treatment

Treatment:

- **Laparoscopic ablation** for stages I and II
- **Surgery** for stages III and IV
- **Clomiphene** citrate and intrauterine insemination (IUI)
- **Gonadotrophins** and IUI
- **IVF**



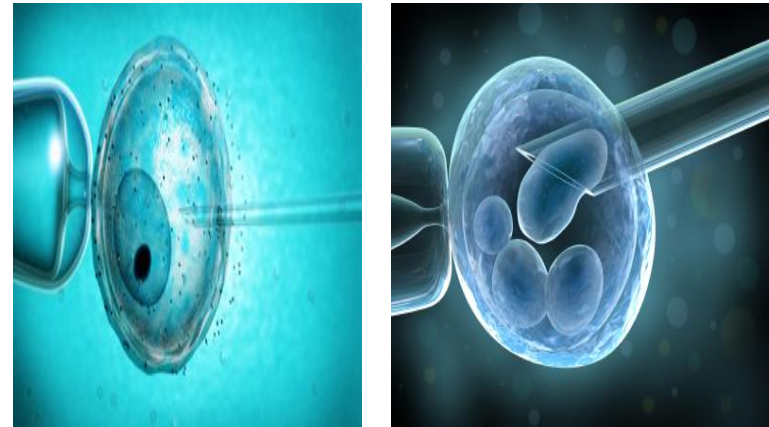
Treatment of Male infertility

Male disorders

- Azoospermia
- Oligozoospermia

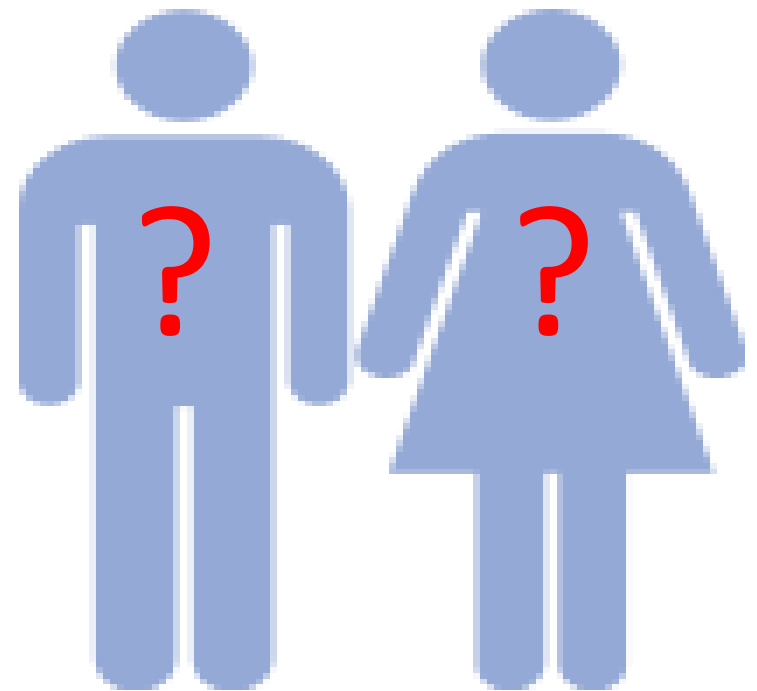
Treatment:

- IUI, partner
- *Donor insemination (in western countries only)*
- IVF and Intracytoplasmic sperm injection (ICSI)



Treatment of Unexplained infertility

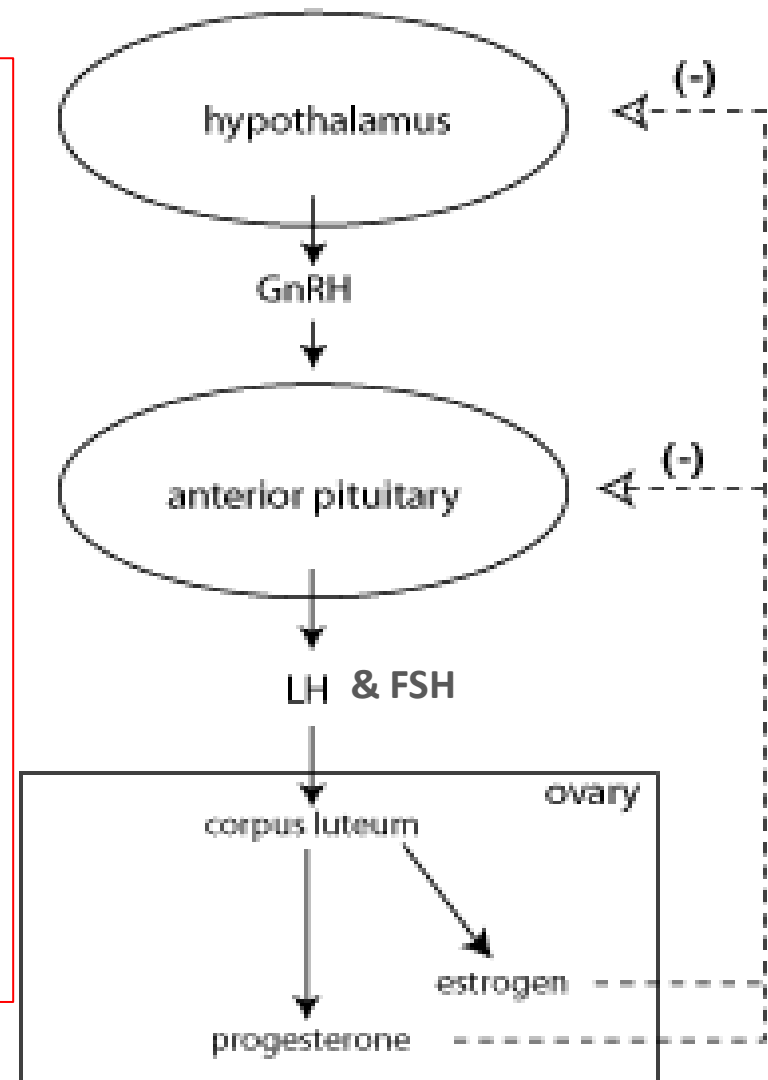
- Clomiphene citrate and IUI
- Gonadotrophins and IUI
- IVF



Clomiphene

- Is a **nonsteroidal estrogen antagonist** that ↑ follicle-stimulating hormone (FSH) and ↑ luteinizing hormone (LH) levels by **blocking estrogen negative feedback at the hypothalamus**

→ **stimulate Ovulation**



Clomiphene

- It induce ovulation in $\approx 60\%$ of women with PCOS and is the initial treatment of choice
- It is less successful in patient with hypogonadotropic hypogonadism

Adverse effects:

- Ovarian hyperstimulation resulting in multiple pregnancy
- Ovarian cysts
- Hot flushes
- Headache
- Increase appetite, weight gain
- Skin rashes

Uses:

1. Infertility
2. *In-vitro* fertilization



Gonadotropins

- Luteinizing hormone, **LH** and Follicle-stimulating hormone, **FSH**
- The gonadotropins are glycoproteins that are produced in the anterior pituitary
- The regulation of gonadal steroid hormones depends on these agents



Gonadotropins

In women:

- **LH** increase estrogen production in the ovary and is required for progesterone production by the corpus luteum after ovulation
- **FSH** is required for normal development and maturation of the ovarian follicles

In men:

- **LH** induces testosterone production by the interstitial (Leydig) cells of the testis
- **FSH** acts on the testis to stimulate spermatogenesis and the synthesis of androgen binding protein

Gonadotropins

Gonadotropine preparations

***All of these hormones are injected IM**

FSH and LH preparations*

Menotropins, hMG (human Menopausal Gonadotrophins), mixture of FSH and LH prepared from human urine collected from postmenopausal women

FSH preparations*

Urinary preparations

Urofollitropin:
- Purified urinary FSH
- Highly purified urinary FSH

Recombinant preparations

-Follitropin alfa
-Follitropin beta

hCG (human Chorionic Gonadotropin)* preparations, is a LH agonist

Urinary preparations

(human) chorionic gonadotropin

Recombinant preparations

choriogonadotropin alfa (recombinant human Chorionic Gonadotropin, r-hCG)

Gonadotropins

- **Uses:**

1. **Menotropine** are used in combination with **hCG** to **stimulate ovulation in women with functioning ovaries**
2. **hCG** can be used in both men and women to stimulate gonadal steroidogenesis in **cases of LH insufficiency**
3. **hCG** can be used to induce external sexual maturation and spermatogenesis in **men with secondary hypogonadism**

- **Adverse effects:**

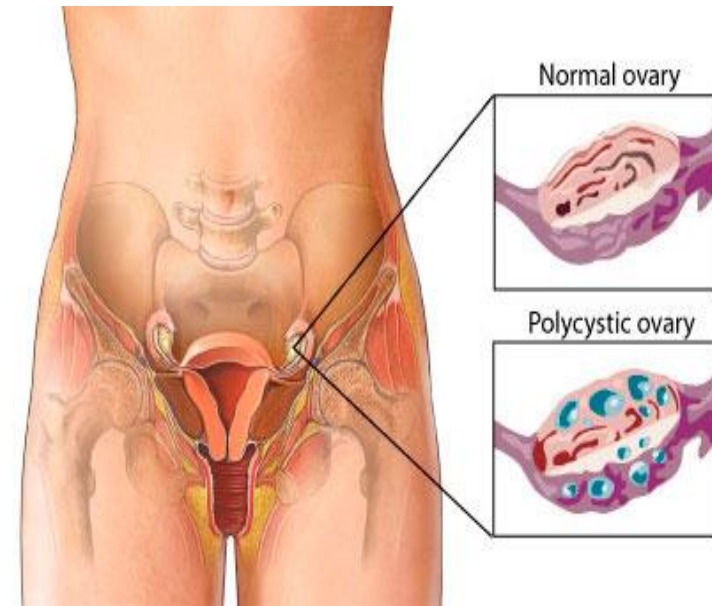
- ✓ Ovarian enlargement
- ✓ Ovarian hyperstimulation syndrome resulting in acute respiratory distress, ascites, hypovolemia and shock
- ✓ Multiple births are not uncommon
- ✓ Men may develop gynecomastia

Metformin

- Is an insulin sensitizer
- it increases glucose uptake and utilization by target tissues, ↓insulin resistance

Uses:

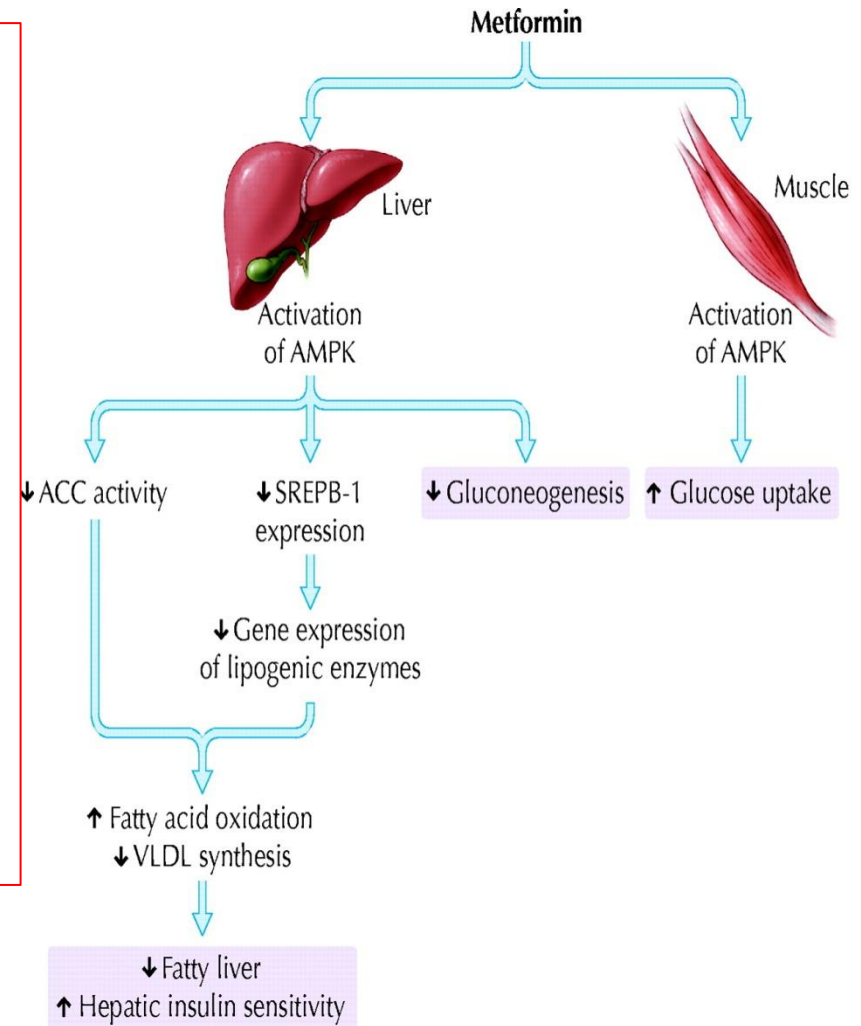
- metformin is effective in the treatment of **polycystic ovary disease**. Its ability to lower insulin resistance in these women can result in ovulation and, possibly, pregnancy



Metformin

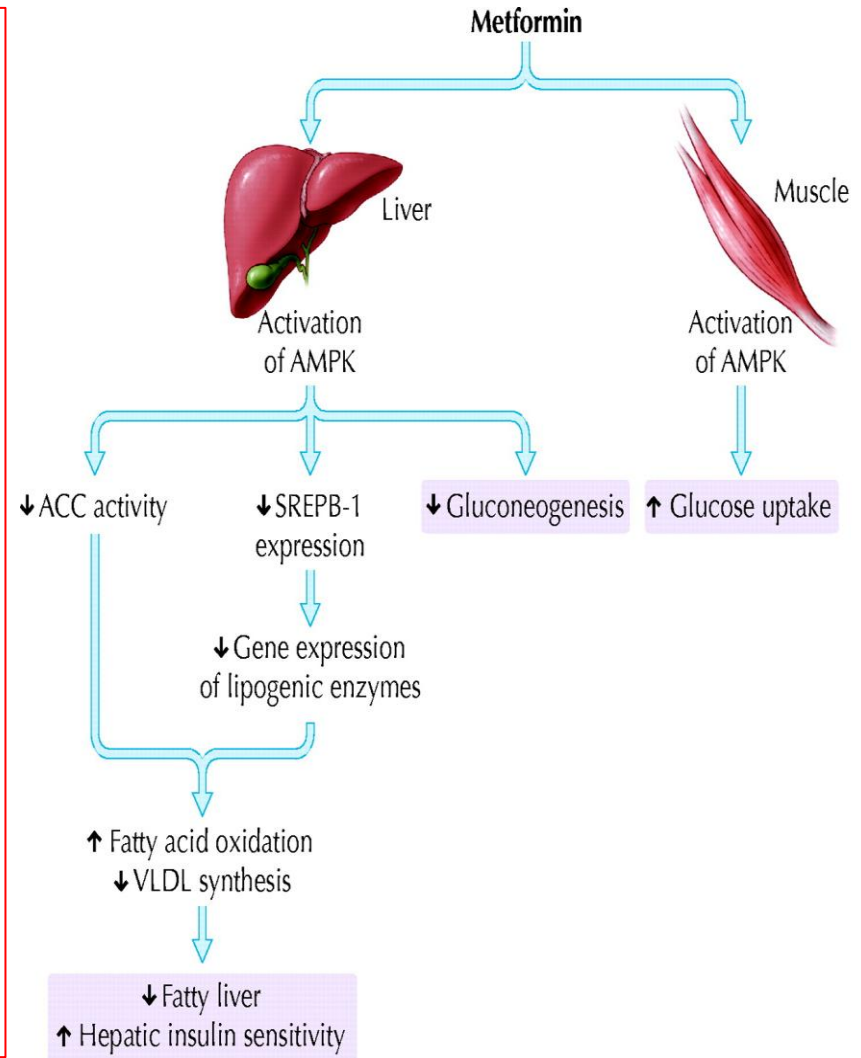
MOA:

- The main action is reduction of hepatic glucose output, by **inhibiting hepatic gluconeogenesis**
- **Inhibit glucose absorption** from the intestine
- Improves peripheral **glucose uptake and utilization**



Metformin

- A very important property of this drug is its ability to **modestly reduce hyperlipidemia** :
 - ✓ ↓ LDL
 - ✓ ↓ VLDL
- These effects may not be apparent until 4 to 6 weeks of use
- The patient often **loses weight** because of loss of appetite
- Metformin as the drug of choice for newly diagnosed Type 2 diabetics



Metformin

Adverse effects:

1. **Lactic acidosis** (rare but serious)
2. Metallic taste
3. Reduce appetite (but anorexia is advantage as it helps in reduction of body weight)

Contraindicated in:

1. Renal disease
2. Hepatic disease
3. Acute myocardial infarction
4. Severe infection
5. Diabetic ketoacidosis

Caution in:

1. Patient with history of congestive heart failure
2. Alcohol abuse

(because of an increased risk of lactic acidosis)

Bromocriptine

- It is a **dopamine D2 receptor agonists**
- That inhibit prolactin secretion by the pituitary
- **Use:**
 1. **Female infertility secondary to hyperprolactinemia**
 2. Amenorrhea
 3. Galactorrhea
 4. Prolactin- secreting tumours
 5. Parkinson disease

Adverse effects:

- Nausea, constipation and headache (common)
- Hypotension
- Drowsiness
- Increase libido and hypersexuality





